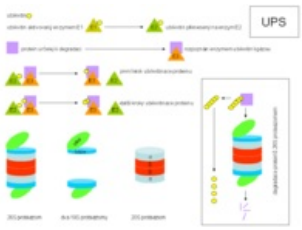
Ubiquitination

Ubiquitination processes



1. Ubiquitin is first bound (activated) in the cell after consumption of ATP by the so-called **ubiquitin-activating enzyme E1**.
2. It is subsequently transferred to the ubiquitin-transferring (or ubiquitin-conjugating) **enzyme E2**.
3. Further transfer of ubiquitin to the **protein to be degraded** (hereafter PDG; or to the nascent ubiquitin chain on PDG) is conditioned by the **E3 ubiquitin ligase** which can specifically recognize proteins to be degraded.

In other words, the E1 and E2 enzymes mainly serve only to transport ubiquitins, while the E3 enzymes handle their final attachment to PDG, recognized by these enzymes. First, the first ubiquitin is bound to the PDG, then the second, the second, the third, etc. The fact that E3 enzymes specifically recognize different PDGs also means that there are few different E1s in cells (according to [1] there are at least two E1 enzymes, namely Uba6 and Ube1) and E2 enzymes in human cells, while there are a diverse number (hundreds) of E3 enzymes for different groups of proteins destined for degradation.

Ubiquitin-ligases

We recognize two basic genera of ubiquitin ligases, which differ in the presence of an active domain: either they contain a **HECT domain** (homologous to E6-Associated Protein C-Terminus), or a **RING domain** (really interesting new gene) [2] [3]. Moreover, in addition to the classic E1-E2-E3 cascade, we now also know the so-called E4 enzymes, which can participate in the extension of the polyubiquitin chain[4].

Binding mode of ubiquitins

A key question is also how the ubiquitins are connected to each other in the chain. Not every polyubiquitin chain is **prima facie** the kiss of death. The most common way of linking two ubiquitins in a polyubiquitin chain is through **lysine 48** (so-called K48 chains) or **lysine 63** (so-called K63 chains), but there are also ubiquitin chains linked through lysine 6, 11, 27, 29 or 33, exceptionally these chains are also branched[5]. Today we cannot say exactly what the meaning of the whole variety of these signals is. K48 chains in particular are considered to be the "kiss of death", while K63 chains mainly play other roles in cell signaling. However, it has recently been shown that proteins tagged with K63 chains can also be recognized by proteasomes and degraded in them[6].There is even the possibility that K63 chains can be converted directly on the tagged protein to K48 chains[7].

Links

Related Articles

- Proteins
- Protein degradation
- Deubiquitination
- History of the ubiquitin-proteasome system
- Proteasome
- Proteasome inhibitors
- Translation

External links

- Ubiquitination (Czech Wikipedia)
- Posttranslational modification (English Wikipedia)

Ubiquitin Proteasome System (https://www.youtube.com/watch?v=hvNJ3yWZQbE) - YouTube video explanation (English)

Source

- CVEK, Boris. From ubiquitin to antabuse. *Britské listy: a daily about everything that is not talked about much in the Czech Republic* [online]. 2011, y. -, p. -, Available from <https://blisty.ca external links>. ISSN 1213-1792.

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